Analysis of homocysteine metabolism enzyme gene polymorphisms in non-syndromic congenital heart disease patients among Malaysians

ABSTRACT

Congenital heart disease (CHD) mainly is caused by the incomplete development of the heart during the first 6 weeks of pregnancy. Chromosomal and genetic abnormalities in the child and high levels of homocysteine in the blood are some of the risk factors related to CHD. Several studies in various populations have been done to determine the candidate genes in the predisposition to CHD with contradictory results, but there have been no studies that had been found in Malaysian CHD patients on homocysteine gene polymorphisms. Hence, this study was conducted to determine the allelic and genotypic analysis of the polymorphisms in candidate genes of the homocysteine enzymes; Methylenetetrahydrofolate Reductase (MTHFR), Cystathionine-b-synthase (CBS), Methionine Synthase (MTR) and Methionine Synthase Reductase (MTRR) genes. Based on the inclusion and exclusion criteria, buccal or blood samples were collected from 150 Malaysian non-syndromic CHD patients and 150 samples from healthy subjects as controls with no matching of age, genders and race between cases and controls. Genomic DNA was extracted from the samples using commercially available kits and the genotyping analysis for C677T MTHFR, A1298C MTHFR, A66G MTRR, A2756G MTR and 844ins68 CBS gene polymorphisms were analyzed using PCR-RFLP analysis. There was a significant difference observed in MTHFR A1298C gene polymorphism between cases and controls (P=0.008). However, there was no significant difference was observed for MTHFR C677T, MTRR A66G, MTR A2756G and CBS 844ins68 gene polymorphism. The association of MTHFR A1298C with the development of CHD in this study emphasis the role of MTHFR gene in the pathogenesis of non-syndromic CHD in Malaysian subjects.

Keyword: Congenital heart disease; MTHFR; MTRR; MTR; Gene polymorphism